Serial No.: 09/829,872 Confirmation No.: 7416 Filed: April 10, 2001

For: NUCLEAR MAGNETIC RESONANCE METHODS FOR IDENTIFYING SITES IN PAPILLOMAVIRUS E2

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Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (Currently Amended) A nuclear magnetic resonance method for identifying a site in a DNA-binding and dimerization domain of [[a]] an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first set of chemical shifts for atoms of a mixture comprising a ligand and the <u>HPV-18 strain of</u> papillomavirus E2 protein; <u>wherein the chemical shifts are assigned to atoms</u> of the protein;

comparing the first set of chemical shifts to a second set of chemical shifts as listed in Table 1; and

identifying at least a portion of the atoms that exhibit changes in chemical shifts, wherein the site comprises the identified atoms.

2. (Currently Amended) The method of claim 1 wherein providing the first set of chemical shifts comprises:

providing a mixture of the ligand and the <u>HPV-18 strain of</u> papillomavirus E2 protein; allowing the ligand to interact with the <u>HPV-18 strain of</u> papillomavirus E2 protein; obtaining a nuclear magnetic resonance spectrum of the mixture; and measuring chemical shifts of atoms from the spectrum.

- 3. (Original) The method of claim 2 wherein allowing the ligand to interact comprises allowing the ligand and the protein to reach a binding equilibrium.
- 4. (Original) The method of claim 1 wherein the site is a ligand binding site.

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5. (Canceled)

- 6. (Currently Amended) The method of claim 1 wherein identifying at least a portion of the atoms comprises indentifying identifying at least one proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.
- 7. (Original) The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one carbon atom that either exhibits a change in ¹³C chemical shift of at least about 0.2 ppm or is no longer observed.
- 8. (Original) The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.
- 9. (Withdrawn-Currently Amended) A nuclear magnetic resonance method for identifying a site in a DNA-binding and dimerization domain of [[a]] an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first ¹H-¹⁵N heteronuclear single quantum correlation spectrum of a mixture comprising a ligand and the <u>HPV-18 strain of</u> papillomavirus E2 protein;

comparing the first ¹H-¹⁵N heteronuclear single quantum correlation spectrum to a second ¹H-¹⁵N heteronuclear single quantum correlation spectrum as illustrated in Figure 2; and identifying at least a portion of the amino acids having atoms that exhibit changes in chemical shifts, wherein the site comprises the identified amino acids.

10. (Withdrawn-Currently Amended) The method of claim 9 wherein providing the first spectrum comprises:

providing a mixture of the ligand and the HPV-18 strain of papillomavirus E2 protein;

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allowing the ligand to interact with the <u>HPV-18 strain of</u> papillomavirus E2 protein; and obtaining a ¹H-¹⁵N heteronuclear single quantum correlation spectrum of the mixture.

- 11. (Withdrawn) The method of claim 10 wherein allowing the ligand to interact comprises allowing the ligand and the protein to reach a binding equilibrium.
- 12. (Withdrawn) The method of claim 9 wherein the site is a ligand binding site.
- 13. (Canceled)
- 14. (Withdrawn) The method of claim 9 wherein identifying at least a portion of the amino acids comprises identifying at least one amino acid having a proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.
- 15. (Withdrawn) The method of claim 9 wherein identifying at least a portion of the amino acids comprises identifying at least one amino acid having a nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.
- 16. (Canceled)
- 17. (Currently Amended) A computer-assisted method for identifying a ligand binding site in a DNA-binding and dimerization domain of [[a]] an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first set of nuclear magnetic resonance chemical shifts for atoms of a mixture comprising the ligand and the <u>HPV-18 strain of</u> papillomavirus E2 protein; wherein the chemical shifts are assigned to atoms of the protein;

causing the first set of chemical shifts to be entered into memory of a computer;

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causing the computer to read a second set of chemical shifts as listed in Table 1 from a machine-readable data storage medium;

causing the computer to compare the first and second sets of chemical shifts; and causing the computer to identify at least a portion of the atoms that exhibit changes in chemical shifts, wherein the ligand binding site comprises the identified atoms.

18. (Canceled)

- 19. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify at least one proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.
- 20. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify at least one carbon atom that either exhibits a change in ¹³C chemical shift of at least about 0.2 ppm or is no longer observed.
- 21. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify a nitrogen atom that either exhibits à change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.
- 22. (Original) The method of claim 17 further comprising causing the computer to visually display a spatial arrangement of atoms of the ligand binding site.